

WHAT IS CLAIMED IS:

1. A method of enhancing cellular proliferation, the method comprising introducing into a cell a compound that alters the expression or activity of a Histone Nuclear Factor P (HiNF-P) polypeptide, in an amount effective to enhance proliferation of the cell.
- 5 2. The method of claim 1, wherein the compound is a nucleic acid molecule comprising a sequence encoding a HiNF-P polypeptide, which is introduced into the cell under conditions such that the HiNF-P polypeptide is expressed.
3. The method of claim 2, wherein the nucleic acid molecule encoding the HiNF-P polypeptide is in an expression vector.
- 10 4. The method of claim 1, wherein the compound is an HiNF-P polypeptide.
5. The method of claim 1, wherein the compound increases the number of HiNF-P polypeptides.
6. The method of claim 5, wherein the activity that is altered results in enhanced expression of a histone H4 gene.
- 15 7. The method of claim 1, wherein the cell is a cultured cell.
8. The method of claim 1, wherein the cell is in a living mammal.
9. The method of claim 8, wherein the living mammal is a human.
10. The method of claim 1, further comprising introducing into the cell a nucleic acid molecule encoding an Nuclear Protein, Ataxia-Telangiectasia locus (NPAT) polypeptide, under conditions such that the NPAT polypeptide is expressed.
- 20 11. The method of claim 10, wherein the nucleic acid molecule encoding the NPAT polypeptide is in an expression vector.
12. The method of claim 8, wherein the mammal has a condition that would benefit from increased cell proliferation.
- 25 13. The method of claim 12, wherein the condition is a wound, and the compound enhances healing of the wound.

14. A method of increasing transcription of a pre-selected target nucleic acid sequence in a cell, the method comprising:

introducing an expression vector into a cell, the vector comprising a Histone Nuclear Factor P (HiNF-P) binding site operatively linked to the target sequence and a regulatory element effective to enable transcription of the target nucleic acid sequence in the cell when a HiNF-P polypeptide is expressed in the cell; and

culturing the cell or progeny of the cell under conditions that enable expression of the HiNF-P polypeptide, thereby increasing transcription of the target nucleic acid sequence.

15. The method of claim 14, wherein the HiNF-P binding site comprises a Site II promoter sequence.

16. The method of claim 14, wherein the vector comprises at least two copies of the HiNF-P binding site.

17. The method of claim 14, wherein the transcribed nucleic acid sequence is translated.

18. The method of claim 14, further comprising introducing into the cell an expression vector comprising a nucleic acid sequence encoding a HiNF-P polypeptide, and culturing the cell to express the HiNF-P polypeptide.

19. The method of claim 14, further comprising introducing into the cell an expression vector comprising a nucleic acid sequence encoding a Nuclear Protein, Ataxia-Telangiectasia locus (NPAT) polypeptide, and culturing the cell to express the NPAT polypeptide.

20. An isolated polypeptide comprising a sequence selected from the group consisting of VRYESVELTQQLLRQPQE (SEQ ID NO:3) and MEKLQGIAEE PEIQMV (SEQ ID NO:4).

21. An isolated antibody or portion thereof that specifically binds to a Histone Nuclear Factor P (HiNF-P) polypeptide.

22. The isolated antibody of claim 21, wherein the antibody specifically binds to an amino acid sequence selected from the group consisting of VRYESVELTQQLLRQPQE (SEQ ID NO:3) and MEKLQGLAEPEIQMV (SEQ ID NO:4).

23. A method of identifying a compound that modulates expression of an H4 histone gene, the method comprising:

obtaining a cell comprising:

(a) a reporter gene operatively linked to a Histone Nuclear Factor P (HiNF-P) binding site, such that when a HiNF-P polypeptide binds to the HiNF-P binding site the reporter gene is expressed, and

(b) a nucleic acid sequence encoding a HiNF-P polypeptide that is expressed;

contacting the cell with a test compound; and

measuring the level of expression of the reporter gene,

wherein a difference in the level of expression of the reporter gene relative to a control cell that was not contacted with the test compound indicates that the test compound modulates the expression of a H4 histone gene.

24. The method of claim 23, wherein the reporter gene is an H4 histone gene.

25. The method of claim 23, wherein the HiNF-P binding site is a Site II promoter sequence.

26. The method of claim 23, wherein expression of the reporter gene is increased relative to the control.

27. The method of claim 23, wherein expression of the reporter gene is decreased relative to the control.

28. The method of claim 23, wherein the test compound is selected from the group consisting of an antisense oligonucleotide and an siRNA.

29. The method of claim 23, wherein the test compound is a peptidomimetic, peptoid, aptamer, carbohydrate, polysaccharide, non-nucleic acid small organic molecule, inorganic molecule, polypeptide, antibody, or ribozyme.

30. An isolated antisense nucleic acid that inhibits expression of a Histone Nuclear Factor P (HiNF-P) polypeptide.

31. The isolated antisense nucleic acid of claim 30, comprising the sequence 5'-GGCATTGGTCTGATTACC-3' (SEQ ID NO:10).

32. A method of decreasing proliferation of a cell, the method comprising:

administering to the cell a composition in an amount sufficient to inhibit Histone Nuclear Factor P (HiNF-P) expression or activity in the cell, thereby decreasing proliferation of the cell.

33. The method of claim 32, wherein the compound administered to the cell is a HiNF-P antisense oligonucleotide.

34. The method of claim 32, wherein the compound administered to the cell is an siRNA that is targeted to a HiNF-P nucleic acid sequence.

35. The method of claim 32, further comprising administering a second composition in an amount sufficient to inhibit Nuclear Protein, Ataxia-Telangiectasia locus (NPAT) expression or activity.

36. A method for detecting a Histone Nuclear Factor P (HiNF-P) polypeptide in a biological sample, the method comprising:

obtaining a biological sample,

contacting the biological sample with an antibody that specifically binds to a HiNF-P polypeptide under conditions that enable the formation of a HiNF-P polypeptide-antibody complex; and

detecting any HiNF-P polypeptide-antibody complexes, wherein the presence of a complex indicates the presence of a HiNF-P polypeptide in the sample.

37. A method of treating a subject having a disorder characterized by excessive cell proliferation, the method comprising administering to the subject a compound that inhibits Histone Nuclear Factor P (HiNF-P) expression or activity, in an amount effective to decrease cell proliferation.

5 38. The method of claim 37, wherein the disorder is cancer.

39. The method of claim 37, wherein the compound administered to the subject is a HiNF-P antisense oligonucleotide.

40. The method of claim 37, wherein the compound administered to the subject is an siRNA that is targeted to a HiNF-P nucleic acid sequence.

10 41. A transgenic non-human mammal whose somatic and germ cells comprise a disrupted Histone Nuclear Factor P (HiNF-P) allele, wherein the cells, if the mouse is homozygous, exhibit decreased HiNF-P activity as compared to a wildtype mouse.

42. The transgenic non-human mammal of claim 41, wherein the mammal is a mouse.

15 43. The transgenic mouse of claim 42, whose cells comprise two disrupted HiNF-P alleles.

44. The transgenic mouse of claim 42, whose cells additionally comprise a disrupted Nuclear Protein, Ataxia-Telangiectasia locus (NPAT) allele.

20 45. A transgenic mouse whose cells comprise a conditional transgene that modulates the expression of a Histone Nuclear Factor P (HiNF-P) polypeptide, wherein under pre-selected conditions the transgene increases or decreases the expression of the HiNF-P polypeptide.

46. The transgenic mouse of claim 45, wherein the conditional transgene decreases the expression of the HiNF-P polypeptide.

25 47. The transgenic mouse of claim 45, wherein the conditional transgene increases the expression of the HiNF-P polypeptide.

48. A targeting vector comprising a nucleic acid sequence that disrupts expression of a Histone Nuclear Factor P (HiNF-P) polypeptide when introduced into a cell, the vector comprising a first and second sequences complementary to first and second

regions of a nucleic acid sequence encoding a HiNF-P polypeptide, and a third sequence inserted between the first and second sequences, wherein the third sequence is not complementary to a nucleic acid sequence encoding a HiNF-P polypeptide.

49. The targeting vector of claim 48, wherein the third sequence is a reporter gene.

5 50. The targeting vector of claim 49, wherein the reporter gene encodes  $\beta$ -galactosidase.

51. The targeting vector of claim 48, wherein the nucleic acid sequence disrupts expression of a HiNF-P polypeptide by homologous recombination into an endogenous HiNF-P allele.

10 52. The targeting vector of claim 48, further comprising a regulatory sequence capable of conditionally disrupting expression of a HiNF-P allele.

53. The targeting vector of claim 52, wherein the regulatory sequence is a Lox sequence.